PLT Docket 97N-0289

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May 19, 1999

Rose E. Cunningham
Project Manager, Pregnancy Labeling Task Force
Center for Drug Evaluation and Research
Food and Drug Administration
56 Fishers Lane
Rockville, MD, 20857

Re: 1. Your kind letter of May 10, 1999.
2. The FDA for Drugs Use-in-Pregnancy [Title 21 CFR 201.57]. . . ought to continue to maintain the trust of **category D** with an unequivocal and strong proviso. . . ***". . . if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective."***

Dear Ms. Cunningham:

Please allow me to thank you for your very kind letter of May 10. It is really a pleasure and an honor to read that my letter has been forwarded to the "*official docket and the chair of the Task Force.*" Also, I really appreciate your information: ". . .*the pregnancy labeling categories should be eliminated and replaced with something more informative*," but I am hopeful that this exercise *does not dilute* the clear, unequivocal, and to the point message of category D. Particularly, the present category D is in accordance to Title 21 CFR 201.57 and *delivers* a clear, unequivocal, and to the point strong proviso: . . *to treat serious disease in pregnant women,* and specifically ". . . *if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective.*" In my opinion, the new language adapted by the FDA that could be '*more informative*' . . . to replace the soon defunct category D, and at the same time, it does fall short in spelling out the clear, unequivocal, and to the point strong proviso, then I believe that we have a "**tragedy**" on the making!

In the course of my research of barbiturates, and particularly Secobarbital/Seconal, in normal pregnancy, and in the context of a prenatal obstetrical analgesic, I believe that I have indirectly been a volunteer and a good-will-ambassador for the Food and Drug Administration. I have been fortunate to present to key publishers of the drug reference industry relevant observations and recommendations, so that they would adapt the strong proviso of category D, for drugs used in pregnancy, i.e., . . *if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective.*" I am very happy to report to you that the following '*icons*' of the Health Care Industry have courageously **accepted** and **implemented** my recommendation [Please compare their 1998 editions to the ones of 1999, with the exception of Drug Facts and Comparisons, where the change will take place for the edition of the year 2000, as per their Managing Editor] and they are:

- United States Pharmacopeial Convention/Micromex's United States Pharmacopeia Dispensing Information (USP DI);
- Facts and Comparisons' Drug Facts and Comparisons;
- Medical Economincs's Physicians' Desk Reference (PDR);
- Mosby's GenRx the Complete Reference of Generic and Brand Drugs;
- Springhouse's Physician Drug Handbook;
- S.W. Saunders' Nursing Drug Handbook;
- PDR/Delmar's Nurse Drug Guide. .

In addition, we do not want to forget that already other '*icons*' in the American drug/medical landscape (please

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note that this ought to be considered a partial listing) have all along adopted the strong proviso for category D, i.e., "... *if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective,*" and they are:

- Merck's Merck Manual of Diagnosis and Therapy [1999];
- Appleton & Lange's Health Professional Drug Guide [1999];
- Appleton & Lange's Pharmacotherapy--A Pathophysiologic Approach [1997];
- Mosby's Nurse Drug Guide [1999].

I believe that my recommendation for a strong proviso for the present category D, i.e., "... *if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective,*" which was courageously **accepted** and **implemented** by USP DI, Drug Facts and Comparisons (in their next edition,) PDR, Mosby, etc., as well as has been all along a standard strong warning for other benchmark medical publishers such as Merck and Appleton & Lange, etc., undoubtedly these testimonials tell us that this critical concern must be regarded and viewed with the utmost attention from all of us, because of the critical impact on the unborn's well-being.

As I have indicated in my letter of April 22, I understand that Title 21 CFR 201.57 principally addresses the '*teratogenic*' issue for drugs' use-in-pregnancy, and I am also aware that Title 21 USC 829--Prescriptions, for schedule II addresses the '*high potential for abuse, physical and psychological dependence*,' but it is also true that conventional wisdom dictates that category D drugs and/or schedule II substances, i.e., barbiturates (and Secobarbital/Seconal being one,) in Pregnancy must be prescribed *'to treat serious disease'* in pregnant women, and for that matter, *'oral prescriptions/orders'* must be prescribed ***only*** and ***if*** needed in a *genuine emergency* and in a *limited quantity*, and not exploited as ***reckless 'parking' contraptions***, in the middle of the night so that the 'obstetrician' can stay in bed, because the dreadful reality of '*respiratory*' and '*vasomotor*' *depression!* A strong proviso for barbiturates in the context of use-in-pregnancy ("... *if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective*") indirectly and compassionately would address other significant concerns such as the directive of Tile 21 USC Section 829--Prescriptions, i.e.,'*oral prescriptions/orders*' must be prescribed ***only*** and ***if*** needed in a *genuine emergency* and in a *limited quantity*, as well as it would address the dreadful reality of '*respiratory*' and '*vasomotor*' *depression* issue.

Now, you could ask me why am I doing all this volunteer and ambassador-labor-of-love for the FDA? The answer is very simple. Again, to critically highlight and to make sure that barbiturates, and particularly Secobarbital/Seconal, in normal pregnancy, and in the context of prenatal obstetrical analgesia [please consider in the middle of the night a scenario where there was no emergency, a *verbal order* of *200 milligrams of Seconal*, a preoperative dosage, where a surgery was required in 1 or 2 hours, and then the 'obstetrician' followed it up after eleven (11) hours, etc. . . .] must be prescribed ***only*** and ***if*** required for *genuine* medical reasons and, again, not exploited as ***reckless 'parking' contraptions*** so that the 'obstetrician' can stay in bed in the middle of the night.

I trust that a clear, unequivocal, and to the point strong proviso to characterize the use of barbiturates in normal pregnancy (and Secobarbital/Seconal being one of them) would be in 'the' best interest for the welfare of the unborn. Again, I would like to reiterate that for barbiturates prescribed in pregnancy the labeling must take into consideration the current strong proviso "... *to treat serious disease in pregnant women.*" In other words, and with the utmost respect, the present strong proviso must never be compromised for the sake of change(s). If I could be of *any* assistance to you or to the chair of the Task Force, please do not hesitate to let me know. Last but not least, please allow me to express my *sincere* gratitude to Dr. Woodcock for her judicious attention. Similarly, I would like to take this opportunity to *genuinely* thank you for your courtesies, time and consideration. Indeed, ***"every unborn's well-being is a sacred trust!"***

Very Truly Yours,

Rosario Zisa, C.P.A.

RZ/

cc: Jane E. Henney, MD, FDA's Commissioner
Donna E. Shalala, Health and Human Service Secretary
Janet Woodcock, MD, Director, FDA's Center for Drug Evaluation and Research